REMARKS

The present application is directed to novel compositions and methods comprising therapeutic delivery compounds. The compounds are particularly suited for the effective delivery of genetic matter and other compounds to the interior of cells. Claims 1-16 were pending prior to the issuance of the January 30, 2003, Non-Final Office Action. Following entry of this amendment claims 1-28 will be pending. Claims 1-5 and 7-16 are amended. New Claims 17-28 have been added. No new matter is added and support for the amendments is found throughout the specification and in the original claims.

Priority

In the January 30, 2003, Office Action the Examiner rejected the claim for priority by the Applicants to their earlier disclosed applications. The Examiner rejected the Applicants' request for priority stating that none of the priority applications recited the combination of a nucleic acid sequence and a polyoxypropylene-polyoxyethylene-polyoxypropylene (POP-POE-POP) linear copolymer. Applicants respectfully submit that Applicants' claimed invention is supported by the priority applications listed in Applicants' claim of priority under 35 U.S.C. §120. Applicants submit that U.S. Application No. 08/138,271 (hereinafter the '271 application) and the applications that derive from this application provide sufficient disclosure of various nucleic acids. Indeed the Applicants' present invention "relates particularly to compositions and methods for treating infectious diseases and genetic disorders through gene therapy and intracellular deliveries of antisense oligonucleotides or other nucleic acid sequences" recited from the '271 application (page 6, lines 1-4) and Example I (page 20, line 2-page 21, line 11). In addition, the '271 application (page 17), in addition to the present application (pages 24 and 26), also cites "Schmolka I.R., *J. Am. Oil Chemist Soc.*, 54:110-116 (1977)," which **discloses the preparation of reverse triblock copolymers** (see Figure 4). This reference is attached as "Exhibit A." Therefore, Applicants respectfully submit that the claimed compositions of the present application, directed to the combination of a reverse triblock copolymer and a nucleic acid sequence or a triplex DNA compound, are supported by the patent applications listed under Applicants'

claim of priority, and that the pending claims should have a priority date of at least October 15, 1993.

Claim objections

In the January 30, 2003, Office Action the Examiner objected to claims 6 and 14 stating that the claims are ungrammatical in regard to the low molecular weight alcohol. Applicants respectfully submit that the claims in questions have now been amended to disclose "a low molecular weight alcohol". Applicants respectfully submit they have overcome the Examiner's objection and request its withdrawal.

Compliance with Sequence Listing Rules

Applicants respectfully submit that a Sequence Listing, for the nucleotide sequence provided on page 34, line 27 of the specification, is enclosed with this response in accordance with 37 C.F.R. 1.821-1.825.

Rejection of Claims 1-16 under 35 U.S.C. §112, First Paragraph (Enablement)

The Examiner rejected Claims 1-16 under 35 U.S.C. §112, first paragraph, as lacking enablement. Applicants respectfully traverse this rejection.

Applicants respectfully submit that claim scope is not limited only to those embodiments disclosed in the specification. One can support broad claims without a single disclosed embodiment. See *Spectra-Physics Inc. v. Coherent Inc., 827 F.2d 1524, 3 U.S.P.Q.2d 1737 (Fed. Cir. 1987).* Moreover, the specification may contain a written description of a broadly claimed invention without describing all species encompassed by the claim. See *Utter v. Hiraga, 845 F.2d 993, 998, 6 U.S.P.Q.2d 1709, 1714 (Fed. Cir. 1988).* Also, "the absence of a working example does not in and of itself compel the conclusion that a specification does not satisfy the requirements of 112." *In re Long, 368 F.2d 892, 895, 151 U.S.P.Q. 640, 642 (C.C.P.A. 1966).*

Applicants' specification discloses compositions containing the recited block copolymers and a compound capable of altering nucleic acid sequence function. Such disclosures are found on the following pages, including, but not limited to, pages 6-8, 11-12 and pages 18-22. The specification also provides that any of the surface active nonionic block

copolymers disclosed can be combined with a variety of compounds capable of altering nucleic acid function (see page 34, lines 3-6). Compounds capable of altering nucleic acid function, including various genes and oligonucleotides, are disclosed on the following pages, including, but not limited to, pages 1-6 and pages 32-40. See also the present specification, page 21, lines 21-23, which provides that the compositions of the present application include, but are not limited to, aqueous solutions, suspensions or emulsions, such as oil-in-water emulsions. The specification also provides that an effective amount of an antisense compound will result in a blood concentration of 1 μM to 100 μM, and that 6 mM to 600 mM of an oligonucleotide concentration is required when 1 ml injections are administered to an average person containing 6.25 liters of blood (see page 34, line 34 – page 35, line 11).

Applicants' specification also discloses that the compositions can be administered by a number of routes including, but not limited to, topical, transdermal, oral, trans-mucosal, subcutaneous injection, intravenous injection, interperitoneal injection and intramuscular injection (see page 10, lines 28-32). Descriptive text of Applicants' claimed methods of delivery can also be found throughout the specification, including, but not limited to, pages 6-8, 11-12 and 18-22.

Applicants submit that the specification teaches that a composition of one or more nucleic acid sequences and block copolymers can be used for therapeutic delivery of nucleic acids to animals, and that both the composition and the methods are enabled by the specification. Applicants teach both ***in vitro*** and ***in vivo*** delivery of nucleic acids sequences using the claimed compositions and methods (see Example IX (page 38) and Example VII (Page 37), respectively.

Applicants have amended claims 1 and 9 to clarify that the composition contains a block copolymer and a nucleic acid sequence or triplex DNA. Therefore, for at least the above reasons, Applicants respectfully submit that Claims 1-16 are enabled by the present specification. Accordingly, Applicants request the withdrawal of the above 112 rejection.

Rejection of Claims 1-16 under 35 U.S.C. §112, First Paragraph (Written Description)

The Examiner rejected Claims 1-16 under 35 U.S.C. §112, first paragraph, as containing subject matter that was not described in the specification in such a way as to

reasonably convey to one skilled in the art that the inventors, at the time the application was filed, had possession of the claimed invention. Applicants respectfully traverse this rejection for the following reasons.

Applicants specification provides sufficient description of the terms "genes," "oligonucleotides," "antisense oligonucleotides," "triplex DNA compounds" and "ribozymes," by using identifying characteristics, functional characteristics and/or descriptive representations. For example, the term "genes" is defined by relevant identifying characteristics and functional characteristics on the following pages of the specification: page 4, lines 2-3 (genes that code for therapeutic compounds); page 17, lines 36-37 (genes that code for the gene product to be immunized against); and page 18, lines 6-7 (genes that code for compounds effective for killing, reducing or retarding cancer). "Oligonucleotides" are defined in term of relevant identifying characteristics and functional characteristics on the following pages of the specification: page 2, lines 24-25 (oligonucleotides that are complimentary to certain gene messages or viral sequences); and page 4, lines 24-26 (oligonucleotides that specifically bind to particular regions of duplex DNA, thereby inactivating the target gene). "Antisense oligonucleotides" are defined in term of relevant identifying characteristics and functional characteristics on the following pages of the specification: page 2, lines 23-26 ("antisense" compounds that are complimentary to certain gene messages or viral sequences); and page 33, lines 3-4 (antisense oligonucleotides use for altering or regulating gene expression and/or protein translation). "Triplex DNA compounds" are defined in term of relevant identifying characteristics and functional characteristics on the following page of the specification: page 4, lines 22-26 (triplex DNA compounds specifically bind to particular regions of duplex DNA to inactivate the target gene). "Ribozymes" are defined in term of relevant identifying characteristics and functional characteristics on page 5, lines 3-8 of the specification (ribozymes are catalytic RNA molecules that consist of a hybridizing region and an enzymatic region).

Applicants also submit that representative examples of "genes" are found on pages 35-37 of the specification (adenosine deaminase gene, gD gene of *Herpes simplex* virus type-1). Representative examples of antisense oligonucleotides are found on page 34, lines 19-23 and lines 24-28 of the specification (antisense oligonucleotides sequence, such as those disclosed

by Matsukura et al. are incorporate by reference; a sequence complimentary to regions of the *art/trs* genes of HIV are prepared according to the method of Matsukura et al.).

An adequate written description of the invention may be shown by any description of sufficient, relevant, identifying characteristics, so long as a person skilled in the art would recognize that the inventor had possession of the claimed invention. MPEP 2163. Moreover, the written description requirement for a claimed genus may be satisfied through sufficient description of a representative number of species ..., or by disclosure of relevant identifying characteristics ..., by functional characteristics coupled with known or disclosed correlation between function and structure, or by a combination of such identifying characteristics, sufficient to show the applicant was in possession of the claimed genus. MPEP 2163.

For at least the above reasons, Applicants respectfully submit that Claims 1-16 are sufficiently described in the specification as to reasonable convey to one skilled in the art that the Applicants, at the time the present application was filed, had possession of the claimed invention. Accordingly, Applicants respectfully request the withdrawal of the above 112 rejection.

Rejection of Claims 1-16 under 35 U.S.C. §112, Second Paragraph

The Examiner rejected Claims 1-16 under 35 U.S.C. §112, second paragraph, as indefinite for failing to particularly point out and distinctly claim the subject matter, which Applicants regard as the invention. The Examiner asserted that Claims 1-16 were indefinite because they recite "human" and "animal" in the alternative, and humans are animals. Applicants have amended Claim 1 to remove both the terms "human" and "animal" and have amended Claim 9 to recite "animal" in place of "human and animal," in accordance with the Examiner's suggestion. Applicants respectfully submit that the term "animal" now refers to both humans and animals. The Examiner found Claims 4 and 12 incomprehensible due to the phrase "the mean aggregate molecular weight of the portion of the wherein". Applicants have amended Claims 4 and 12 to remove this phrase. The Examiner found Claims 5 and 13 indefinite due to the term "genes". Applicants respectfully submit that the term "genes" refers to any gene-encoding sequence, and thus refers to both open reading frame sequences and those sequences adjacent to, or including, one or more noncoding sequences. The Examiner

found Claims 7 and 15 indefinite due to the trademark/trade name "Tween 80". Applicants have amended Claims 7 and 15 to replace the trade name "Tween 80" with its chemical name, polyoxyethylene (20) sorbitan monooleate. The Examiner found Claims 14 and 15 indefinite because it was unclear how these method claims were furthered by including a surfactant or an alcohol, and method Claim 16 indefinite due to the inclusion of an expression vector. Applicants have amended Claims 14, 15 and 16 to provide that the composition used in these method claims, contains the additional respective components. The Examiner also asserted that Claims 1-16 lacked proper antecedent basis for the term "the compound," for example, the phrase "about 40% of the compound by weight." Applicants respectfully submit that this term and related phrases are not recited in Applicants' pending claims.

Therefore, for at least the above reasons, Applicants respectfully assert that Claims 1-16 are definite, and request the withdrawal of this rejection.

Rejection of Claims 1-5 and 9-12 under 35 U.S.C. §102(b)

The Examiner rejected Claims 1-5 and 9-12 under 35 U.S.C. §102(b), as anticipated by U.S. Patent 6,093,391 to Kabanov et al. (hereinafter "Kabanov '391"). Applicants respectfully traverse this rejection for the following reasons.

As explained above, the present invention has a priority date of at least October 15, 1993, and thus, Kabanov '391 cannot be considered as a prior art reference. Therefore, Applicants respectfully request the withdrawal of this rejection.

In addition, Kabanov '391 teaches composition of **peptides** and block copolymers and methods of treatment using these compositions (abstract). Applicants pending claims are directed to compositions containing a block copolymer and one or more **nucleic acid sequences** or one or more triplex DNA compounds and methods of delivering a nucleic acid sequence to an animal using these compositions. Kabanov '391 fails to teach or suggest reverse block copolymers containing a polyoxypropylene portion with a molecular weight of greater than 3100, as claimed in newly added claims 17-19 and 23-25. Moreover, Kabanov '391 fails to teach or suggest reverse block copolymers containing a polyoxyethylene portion that is less than 10% or greater than 80% of the total weight of the block copolymer, as

claimed in newly added claims 21-22 and 27-28. Thus, Applicants submit that Kabanov '391 fails to teach the claimed compositions and methods.

Rejection of Claims 1-4 and 9-12 under 35 U.S.C. §102(b)

The Examiner rejected Claims 1-4 and 9-12 under 35 U.S.C. §102(b), as anticipated by U.S. Patent 5,824,322 to Balasubramanian (hereinafter "Balasubramanian"). Applicants respectfully traverse this rejection for the following reasons.

As mentioned above, the present application has a priority date of at least October 15, 1993, and thus, Balasubramanian cannot be considered as a prior art reference. Therefore, Applicants respectfully request the withdrawal of this rejection.

Moreover, Balasubramanian teaches compositions and methods using only nonionic reverse block copolymers. Balasubramanian fails to teach or suggest compositions containing a reverse block copolymer and one or more **nucleic acid sequences** or one or more triplex DNA compounds. Thus, Balasubramanian fails to teach or suggest Applicants' claimed invention.

Rejection of Claims 1-3 and 9-11 under 35 U.S.C. §102(b)

The Examiner rejected Claims 1-3 and 9-11 under 35 U.S.C. §102(b), as anticipated by U.S. Patent 4,902,500 to Jansen et al. (hereinafter "Jansen"). Applicants respectfully traverse this rejection for the following reasons.

Jansen teaches stable antibody preparations containing a mixture of at least one polyoxypropylene-polyoxyethylene block copolymer **and at least one phospholipid** (abstract). Applicant's pending claims are directed to compositions containing block copolymers and one or more **nucleic acid sequences** or one or more triplex DNA compounds; and related methods of delivering a nucleic acid sequence to an animal using these compositions. Applicants respectfully submit that Jansen fails to teach or suggest compositions containing nucleic acid sequences or triplex DNA compounds, and therefore, does not teach or suggest Applicants' pending claims.

For at least the above reasons, Applicants respectfully submit that Jansen does not anticipate Claims 1-3 and 9-11 and respectfully request the withdrawal of this rejection.

Rejection of Claims 1-5, 8-13 and 16 under 35 U.S.C. §102(e)

The Examiner rejected Claims 1-5, 8-13 and 16 under 35 U.S.C. §102(e), as anticipated by U.S. Patent 6,359,054 to Lemieux et al. (hereinafter "Lemieux"). Applicants respectfully traverse this rejection for the following reasons.

As mentioned above, the present application has a priority date of at least October 15, 1993, and thus, Lemieux cannot be considered as a prior art reference. Applicants respectfully request the withdrawal of this rejection.

In addition, Lemieux fails to teach or suggest reverse block copolymers having a polyoxypropylene portion with a molecular weight of greater than 3100, as claimed in newly added claims 17-19 and 23-25. Moreover, Lemieux fails to teach or suggest reverse block copolymers consisting of a polyoxyethylene portion that is less than 10% or greater than 80% of the total weight of the block copolymer, as claimed in newly added claims 21-22 and 27-28.

Rejection of Claims 4 and 12 under 35 U.S.C. §103(a)

The Examiner rejected Claims 4 and 12 under 35 U.S.C. §103(a), as obvious over U.S. Patent 4,902,500 ("Jansen"). Applicants respectfully traverse this rejection for the following reasons.

As discussed above, Applicants respectfully submit that Jansen fails to teach or suggest compositions containing **nucleic acid sequences** or triplex DNA compounds, and therefore, does not teach or suggest Applicants' pending claims. In addition, Jansen teaches stable antibody preparations containing a mixture of at least one polyoxypropylene-polyoxyethylene block copolymer **and at least one phospholipid** (abstract).

For at least the above reasons, Applicants respectfully submit that Jansen does not teach or suggest Claims 4 and 12, and respectfully request the withdrawal of this rejection.

Rejection of Claims 5 and 8 under 35 U.S.C. §103(a)

The Examiner rejected Claims 5 and 8 under 35 U.S.C. §103(a), as obvious over U.S. Patent 6,093,391 (Kabanov '391) in view of U.S. Patent 5,656,611 (Kabanov '611). Applicants respectfully traverse this rejection for the following reasons.

As mentioned above, the present application has a priority date of at least October 15, 1993, and thus, these references cannot be considered as prior art references. Therefore, Applicants respectfully request the withdrawal of this rejection.

In addition, neither Kabanov '391 or Kabanov '611 teach or suggest the claimed compositions and methods. Both Kabanov '391 and Kabanov '611 fail to teach or suggest reverse block copolymers containing a polyoxypropylene portion with a molecular weight of greater than 3100, as claimed in newly added claims 17-19 and 23-25. Moreover, Kabanov '391 fails to teach reverse block copolymers having a polyoxyethylene portion that is less than 10% or greater than 80% of the total weight of the block copolymer, as claimed in newly added claims 21-22 and 27-28.

Rejection of Claim 13 under 35 U.S.C. §103(a)

The Examiner rejected Claim 13 under 35 U.S.C. §103(a), as obvious over Kabanov '391 and Kabanov '611, in further view of Abe et al. (Biochem. Biophys. Res. Comm. 198(1): 16-24, 1/1994). Applicants respectfully traverse this rejection for the following reasons.

As mentioned above, the present application has a priority date of at least October 15, 1993, and thus, these references cannot be considered as prior art references. Applicants respectfully request the withdrawal of this rejection.

In addition, Applicants pending claims are directed to compositions containing a block copolymer and one or more nucleic acid sequences or one or more triplex DNA compounds and methods of delivering a nucleic acid sequence to an animal using these compositions. Abe et al. (hereinafter "Abe") examines the effect of an antisense oligodeoxynucleotide dissolved in F127 pluronic gel. Abe does not teach or even suggest compositions containing **reverse block copolymers**, and thus, does not teach or suggest the claimed compositions. Both Kabanov '611 and Kabanov '391 fail to teach or suggest block copolymers having a polyoxypropylene portion with a molecular weight of greater than 3100, or block copolymers consisting of a polyoxyethylene portion that is less than 10% or greater than 80% of the total weight of the block copolymer. Thus, Applicants submit that the cited references, either alone or in combination fail to teach the claimed invention.

CONCLUSION

The foregoing is submitted as a full and complete Response to the Non-Final Office Action mailed on January 30, 2003. No new matter is added by these amendments. For at least the reasons given above, Applicants respectfully submit that the pending claims are enabled, fully described, definite, novel and non-obvious. Accordingly, Applicants submit that the claims in the present application are in condition for allowance, and such action is courteously solicited.

Checks for a three month petition for extension of time and for the petition to revive are included herewith. The Commissioner is hereby authorized to charge any deficiency, or credit any overpayment, to Deposit Account No. 11-0855.

The Examiner is invited and encouraged to contact the undersigned attorney of record at telephone number listed below, if such contact will facilitate an efficient examination and allowance of the application.

Respectfully submitted.

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